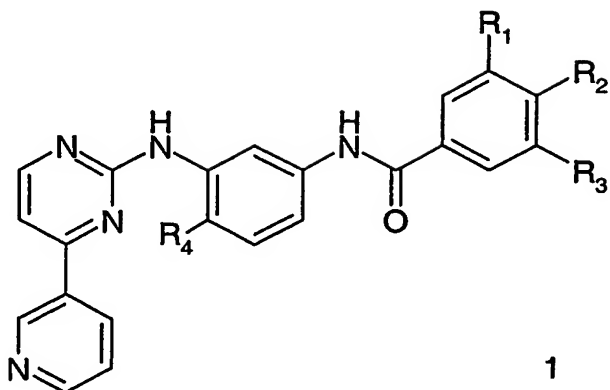


WHAT IS CLAIMED IS:

1. A compound of formula 1



wherein

R_1 represents hydrogen and R_2 represents NR_5R_6 , or R_1 represents NR_5R_6 and R_2 represents hydrogen;

R_3 represents lower alkyl, fluoroalkyl, hydroxyalkyl or carbamoyl;

R_4 represents hydrogen, lower alkyl or halogen; and

R_5 and R_6 represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxy-carbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or lower acyl, or R_5R_6 together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

2. A compound of formula 1 according to claim 1 wherein

R_1 represents hydrogen and R_2 represents NR_5R_6 , or R_1 represents NR_5R_6 and R_2 represents hydrogen;

R₃ represents lower alkyl, fluoroalkyl, hydroxyalkyl or carbamoyl;

R₄ represents lower alkyl; and

R₅ and R₆ represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or lower acyl, or R₅R₆ together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy; and a N-oxide or a pharmaceutically acceptable salt of such a compound.

3. A compound of formula 1 according to claim 1 wherein

R₁ represents hydrogen and R₂ represents NR₅R₆, or R₁ represents NR₅R₆ and R₂ represents hydrogen;

R₃ represents trifluoromethyl;

R₄ represents methyl; and

R₅ and R₆ represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower acyloxy-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidinyl, N-lower alkylpyrrolidinyl, or acetyl, or R₅R₆ together represent alkylene with four, five or six carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl, hydroxy or lower alkoxy; and a N-oxide or a pharmaceutically acceptable salt of such a compound.

4. A compound of formula 1 according to claim 1 wherein

R₁ represents hydrogen and R₂ represents NR₅R₆, or R₁ represents NR₅R₆ and R₂ represents hydrogen;

R₃ represents trifluoromethyl;

R₄ represents methyl; and

R₅ and R₆ represent, independently of each other, hydrogen, lower alkyl, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidiny, or lower acyl, or R₅R₆ together represent alkylene with four or five carbon atoms, oxa-lower alkylene with one oxygen and three or four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, hydroxy-lower alkyl or lower alkoxy-lower alkyl, and wherein lower alkylene in each case may be partially or totally unsaturated and/or the carbon atoms of lower alkylene may be substituted by lower alkyl; and a N-oxide or a pharmaceutically acceptable salt of such a compound.

5. A compound of formula 1 according to claim 1 wherein

R₁ represents hydrogen and R₂ represents NR₅R₆, or R₁ represents NR₅R₆ and R₂ represents hydrogen;

R₃ represents trifluoromethyl;

R₄ represents methyl; and

R₅ and R₆ represent, independently of each other, hydrogen, lower alkyl, di(lower alkyl)amino-lower alkyl, N-lower alkylpiperidiny, or lower acetyl, or R₅R₆ together represent alkylene with four or five carbon atoms, oxa-lower alkylene with one oxygen and four carbon atoms, or aza-lower alkylene with one nitrogen and three or four carbon atoms wherein the nitrogen atom is unsubstituted or substituted by lower alkyl, and wherein aza-lower alkylene may be unsaturated and/or the carbon atoms of aza-lower alkylene may be substituted by lower alkyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

6. A compound of formula 1 according to claim 1 wherein

R₁ represents hydrogen and R₂ represents NR₅R₆, or R₁ represents NR₅R₆ and R₂ represents hydrogen;

R₃ represents trifluoromethyl;

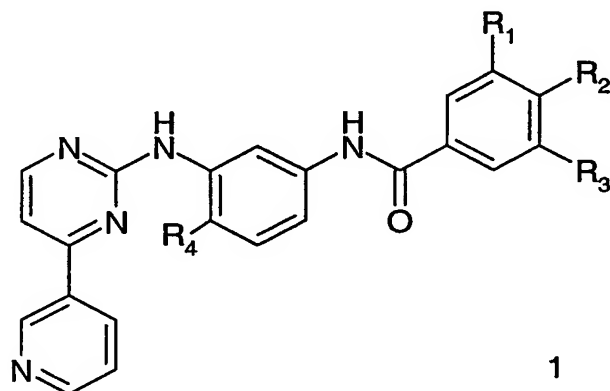
R₄ represents methyl; and

R₅ and R₆ represent, independently of each other, hydrogen, methyl, ethyl, 2-dimethylaminoethyl, 4-methyl-1-piperidiny, or acetyl, or NR₅R₆ together represent pyrrolidino,

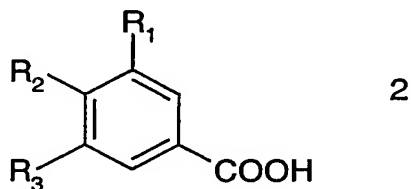
piperidino, morpholino, N-methylpiperazino, 1H-imidazolyl, 1H-2-methylimidazolyl, 1H-4-methylimidazolyl or 1H-2,4-dimethylimidazolyl;

and a N-oxide or a pharmaceutically acceptable salt of such a compound.

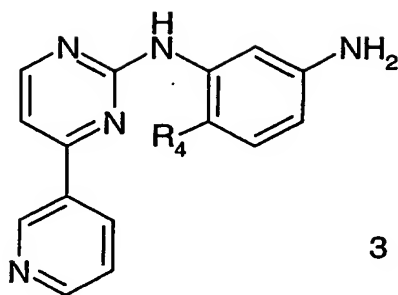
7. A process for the synthesis of a compound of the formula 1



or an N-oxide or a salt thereof, wherein the symbols R_1 , R_2 , R_3 and R_4 are as defined in claim 1, characterized in that a compound of formula 2



wherein R_1 , R_2 and R_3 are as defined for a compound of formula 1, or a derivative thereof wherein the carboxy group $-COOH$ is in activated form, is reacted with an amine of the formula 3



wherein R_4 is as defined for a compound of the formula 1, optionally in the presence of a dehydrating agent and an inert base and/or a suitable catalyst, and optionally in the presence of an inert solvent;

where the above starting compounds of formula 2 and 3 may also be present with functional groups in protected form if necessary and/or in the form of salts, provided a salt-forming group is present and the reaction in salt form is possible;

any protecting groups in a protected derivative of a compound of the formula 1 are removed;

and, if so desired, an obtainable compound of formula 1 is converted into another compound of formula 1 or a N-oxide thereof, a free compound of formula 1 is converted into a salt, an obtainable salt of a compound of formula 1 is converted into the free compound or another salt, and/or a mixture of isomeric compounds of formula 1 is separated into the individual isomers.

8. A pharmaceutical composition comprising as an active ingredient a compound of formula 1 according to claim 1 or a N-oxide or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier.

9. Use of a compound of formula 1 according to any one of claims 1 to 6 or of a N-oxide or a possible tautomer thereof or of a pharmaceutically acceptable salt of such a compound for the preparation of a pharmaceutical composition for the treatment of a disease which responds to an inhibition of protein kinase activity.

10. The use of a compound of formula 1 according to any one of claims 1 to 6 or of a N-oxide or a possible tautomer thereof or of a pharmaceutically acceptable salt of such a compound in the treatment of a disease, which responds to an inhibition of protein kinase activity.

11. A method for the treatment of a disease which responds to an inhibition of protein kinase activity, which comprises administering a compound of formula 1 according to claim 1 or a N-oxide or a pharmaceutically acceptable salt thereof.

12. Use or method according to any one of claims 9 to 11 wherein the disease is a neoplastic disease.

13. Use or method according to any one of claims 9 to 11 wherein the disease is a leukemia which responds to an inhibition of the Raf and/or Abl tyrosine kinase activity.